REMARKS

Claims 1-53 are pending in the application. The Examiner has withdrawn claims 22-52, has rejected claims 1-21 and 53, and has objected to claims 1, 18, and 53. Applicants wish to thank Examiner Royds and SPE Marshall for the courtesy of an interview on May 23, 2006. In this response, Applicants have presently amended claims 1-3, 5-7, 9-20, 31-48, and 53, and have cancelled claims 22-30 and 49-52. As will be explained in greater detail below, although claims 31-48 have been withdrawn by the Examiner as directed to nonelected subject matter (because they recite a process), Applicants submit that recitation is in error as claims 31-48 are actually composition claims, and thus reflect elected subject matter. In view of these amendments, and as discussed below, it is submitted that the application is now in condition for allowance.

Summary of the Invention of the Present Application

The invention of the present application provides a composition including the tannate salts of active pharmaceutical ingredients, such as phenylephrine, pyrilamine, and dextromethorphan. This composition is prepared by a method that enhances the uniformity of the amounts of the active pharmaceutical ingredients in the composition over that found in the prior art. The method of preparing the composition involves a conversion process, including mixing a dispersing agent and tannic acid in a suitable solvent to generate a mixture, referred to as a dispersion. A solution of the active pharmaceutical ingredients, as common salts or in the free base form, is added

slowly to the dispersion to generate tannate salts of the active pharmaceutical ingredients. The tannate salts are directly processed into suitable dosage forms, such as a suspension or tablets. The use of the dispersion prevents the clumping and aggregation of the tannate salt formed. Thus, as the tannate salts are further processed into dosage forms, the dispersion promotes homogeneity of the amount of active pharmaceutical ingredients. Thus, each dosage unit of the dosage form (e.g., each tablet or each 5 ml of suspension) will include an amount of the tannate salts that is generally uniform to each other dosage unit (e.g., each other tablet or 5 ml of suspension). Further, the use of free base or common salt forms of phenylephrine, pyrilamine, and dextromethorphan that are processed directly into tannate salts in the composition in situ, further aids in reducing variability of active pharmaceutical ingredients in final product. This is because there is less variability in the free base or common salts than in the tannate salts. Thus, by starting with a commonly available salt or free base of the active pharmaceutical ingredient, which is subsequently converted and incorporated in situ as a tannate salt complex, the invention provides an efficient and reproducible method to manufacture liquid or semi-solid products containing tannate salt complexes as active ingredients.

As a result of the method used to prepare the compositions, the problem described in the application of prior art pharmaceutical compositions that contain variable, and sometimes sub-therapeutic, levels of active pharmaceutical ingredients is

ameliorated by providing a composition including a generally uniform amount of active pharmaceutical ingredients from dosage unit to dosage unit. Since the tannate salts of phenylephrine, pyrilamine, and/or dextromethorphan are generated and incorporated in situ into the dosage form during the manufacturing process, the purification and drying steps, which are generally required for the isolation of the tannate salts, are also eliminated.

Requirement for Restriction/Election

As described above, the Examiner has withdrawn claims 22-52 from further consideration pursuant to 37 C.F.R. 1.142(b) as being drawn to a nonelected invention. In the Restriction Requirement dated December 5, 2005, the Examiner had required restriction to one of the following inventions under 35 U.S.C. § 121: (1) claims 1-21 and 53, drawn to a composition comprising phenylephrine, pyrilamine, and dextromethorphan, or (2) claims 22-52, drawn to a manufacturing process for a composition comprising phenylephrine, pyrilamine, and dextromethorphan. The Examiner had stated that inventions I and II were related as a process of making and a product made thereby.

In response to the Restriction Requirement, Applicants elected to pursue the composition claims of the application with traverse. Applicants here do not wish to change their decision of pursuing the composition claims, but submit that claims 1-21 and 53 are not the only composition claims of the application. Rather, certain of claims

22-52, which the Examiner placed in Group II as being drawn to a manufacturing process, are, in actuality, composition claims. In particular, independent claim 31 and its dependent claims 32-48 are drawn to composition comprising phenylephrine, pyrilamine, and dextromethorphan. This can be seen in the preamble to independent claim 31, which recites, "A composition comprising." Applicants believe there is confusion as to dependent claims 32-48 because those claims each include a typographical error in reciting a "process" comprising, rather than the correct term, "composition." In view of that typographical error, Applicants have presently amended claims 32-48 to correctly recite a "composition." At the same time, Applicants have also cancelled process claims 22-30 and 49-52 from the application.

Applicants Claim for Priority Under 35 U.S.C. § 120

The Examiner states that Applicants have failed to comply with the conditions for receiving the benefit of an earlier filing date under 35 U.S.C. § 120 because the subject matter disclosed in U.S. Patent Application No. 10/047,578 ("the '578 application") does not contain sufficient support and enablement under 35 U.S.C. § 112, first paragraph, for the presently claimed subject matter. In particular, the Examiner states that the disclosure of the '578 application does not reasonably disclose or suggest a composition comprising phenylephrine, pyrilamine, and dextromethorphan. Accordingly, the Examiner states that Applicants' claim for priority is denied, and the

claims are granted an effective filing date of August 22, 2003 (the filing date of the present application).

Applicants disagree with the Examiner. Applicants submit that claiming the benefit of a prior-filed application under 35 U.S.C. § 120 is a legal matter that is ultimately determined by a comparison of the issued claims to the disclosure of the '578 application. Thus, Applicants submit that such a determination is not within the purview of the Examiner, but rather, will be determined by a Court, should the issue arise. In any event, because there are no issued claims in the present application as of yet, Applicants submit that any discussion of a claim of priority is premature. Applicants therefore request that the denial of the claim for priority be withdrawn.

Objections to the Claims

The Examiner has objected to claims 1 and 53 for reciting, for example, "a." to delineate a step of the process of forming the claimed product. The Examiner states that proper claim construction dictates that only one period should appear at the conclusion of a claim, unless it is used to denote a decimal point in a number within the claim. While not necessarily agreeing with the Examiner's objection, Applicants note that the presently amended claims no longer recite "a.," "b.," etc. to denote steps of the process. Therefore, Applicants submit that this objection has been rendered moot.

The Examiner has also objected to claim 18 for failing to define the acronym "MAS" at its first occurrence in the claims. In response, Applicants have

amended claim 18 to replace the acronym "MAS" with "magnesium aluminum silicate." Applicants therefore submit that the objection to claim 18 has been overcome.

Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

The Examiner has objected to claims 1-13, 16-21, and 53 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention. In particular, the Examiner states that the use of the terms "first solvent," "first solution," "second solvent," "second solution," and "first dispersion," as recited in claim 1, are terms that render the claims indefinite. While Applicants do not agree that the identity of "first" or "second" solvents, "first" or "second" solutions, or a "first" dispersion renders claims indefinite, the claims as presently amended now no longer include those terms. Thus, Applicants submit that these rejections have been rendered moot.

Further, the Examiner has rejected claim 3 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention. In particular, the Examiner states that it is not clear whether the limitation of "the active pharmaceutical ingredients are selected from the group consisting of salts ..." is intended to limit the process as set forth in claim 1 or the composition as set forth in claim 1. In view of the claims as amended, Applicants note that the first listed step in the process of claim 1 recites, "forming a solution by dissolving the salt or free base of the active pharmaceutical

ingredients in a solvent." Thus, Applicants submit that it is clear that the salts recited in claim 3 refer to those salts used in this step of the process of forming the compositions. Applicants therefore submit that the rejection of claim 3 under 35 U.S.C. § 112, second paragraph, has been overcome.

The Examiner has also rejected claims 2, 6-8, and 10-21 under 35 U.S.C. § 112, second paragraph, as being indefinite. In particular, the Examiner states that the term "about" as used in those claims is a relative term that renders the claim indefinite. In response, Applicants have amended claims 2, 6, 7, and 10-20 to remove those occurrences of the term "about." Applicants thus submit that the rejection of claims 2, 6-8, and 10-21 under 35 U.S.C. § 112, second paragraph have been overcome.

Claim Rejections 35 U.S.C. § 102

The Examiner has rejected claims 1, 3-8, 10-18, 21, and 53 under 35 U.S.C. § 102(a) or 102(e) as being unpatentable over U.S. Patent No. 6,509,492 ("Venkataraman"). Applicants respectfully disagree with the rejections. As will be discussed in greater detail below, Applicants submit that Venkataraman does not disclose or suggest a composition that is homogeneous in its active pharmaceutical ingredients. In particular, Applicants submit that a homogeneous composition is produced by method of an in situ conversion of a free base or salt form of the active ingredients to tannate salts to provide a composition in an amount including a plurality of dosage units, which are homogeneous in amounts of the active ingredients from one

unit to the next, as recited in the present claims, is completely different from the composition of Venkataraman.

As an initial matter, Applicants note that only independent claims 1 and 53, and certain claims depending from claim 1, stand rejected. In view of the above discussion regarding the mistaken identification of claims 31-48 as process claims due to a typographical error, Applicants submit that the following arguments directed to composition claims 1, 3-8, 10-18, 21, and 53 apply equally to composition claims 31-48, since independent claim 31 has been presently amended to include the same language regarding a "homogeneous" composition, which Applicants contend distinguishes the claimed composition over that of the cited art.

Turning now to the substance of the presently amended claims: Applicants first submit that independent claims 1 and 53 have each now been amended to recite that the tannate salts are combined with at least one suspending agent to produce a "homogeneous suspension" or produce a "homogeneous composition," including pharmaceutically active salts wherein that suspension or composition includes a plurality of dosage units, and "being homogeneous in amounts of active pharmaceutical ingredients in each of the dosage units when compared with each of the other dosage units." Such a composition is not found in Venkataraman, as will be described in greater detail below.

Applicants further submit that independent claims 1 and 53 include at least two additional recitations in the recited process that render the amounts of active pharmaceutical ingredients homogeneous in the claimed composition, thereby distinguishing the claimed composition from that disclosed in Venkataraman. First, the recited use of a separate dispersion (including a dispersing agent such as magnesium aluminum silicate, xanthan gum, and cellulose compounds) prevents the aggregation of the tannate salts as they precipitate out of solution, thereby enhancing the homogeneity, or uniformity, of amounts of active pharmaceutical ingredients from dosage unit to dosage unit. Second, the recited conversion process begins with the free base or common salt form of the active pharmaceutical ingredients. Such forms exhibit less variability in amounts of active pharmaceutical ingredients, as opposed to the tannate form that is isolated and then used in the cited reference. Thus, by starting with a form having less variability in amounts of the active, the claimed composition prepared in that manner also demonstrates greater uniformity of amounts of active ingredients over the cited reference, once processed in situ into the tannate salt forms. These recitations of the claims will be discussed in greater detail below.

Claims 1 and 53 each recite that the process for preparing the composition involves combining a solution (which includes active pharmaceutical ingredients) to a dispersion (including a dispersing agent and tannic acid). As described above, and throughout the application, the novel process of using a dispersion aids in

increasing the homogeneity (i.e., the uniformity) of the amounts of active pharmaceutical ingredients from batch to batch (and thus dosage unit to dosage unit) of the presently claimed composition, as opposed to the more variable levels of active pharmaceutical ingredients present in compositions of the cited art. Support for this may be found at least at page 4, lines 22-24, page 8, lines 5-6, and page 13, lines 17-19 of the present application. The application, at pages 4, 8, and 13, describes that the presence of the dispersing agent and its use in a separate dispersion (which is not found in the cited art) prevents the clumping and aggregation of the tannate salt formed. Thus, as is described at least at page 12, line 22, through page 13, line 3, this method, by preventing clumping and aggregation of the tannate salt, promotes uniformity of the amounts of active pharmaceutical ingredients in the compositions formed.

Further, as recited in independent claims 1 and 53, the active pharmaceutical ingredient is added in its free base or salt form. This further reduces variability and promotes uniformity of API in final product. At least, at page 3, line 20 through page 4, line 5, the application describes that one problem with present compositions is that the presence of low active percentages of antihistamine or decongestant and the variable purity of commercially available antihistamine and decongestant tannate salts results in the stoichiometry of active free-based tannic acid in the tannate salts being different from batch to batch of compositions prepared. This results in significant dosing and processing problems during manufacturing, and results

in commercially available pharmaceutical compositions that contain variables, and in some instances, subtherapeutic levels of active pharmaceutical ingredients. However, by using the free base or common salt form, as in the method of the present composition claims, the present invention reduces this variability. This, however, is not seen in the cited art. The cited art (Venkataraman) only includes old or conventional processes for preparing compositions including tannate salts, and thus those compositions vary in their amounts of active pharmaceutical ingredients, which is wholly different than the composition recited in the present claims.

Venkataraman only mentions processes for preparing its compositions at two locations. First, at column 2, lines 4-10, Venkataraman states that the compositions can be "compounded in a conventional manner." No more detail than simply reciting this "conventional" method is described at column 2. Second, at column 6, lines 40-43, Venkataraman states that "preparations of tannate compounds in a very pure form are taught by U.S. Patent Nos. 5,599,846 and 5,663,415 to Chopdekar et al., which are herein incorporated in their entireties." The Chopdekar patents do describe, in some detail, the process of preparing tannate compounds.

The Chopdekar patents describe processes for the preparation of tannate forms, for example, of pyrilamine and/or phenylephrine, which may then be used to prepare compositions including those tannate salt forms of phenylephrine and pyrilamine. In other words, the tannate forms are obtained, isolated, and purified, and

then subsequently incorporated into other compositions. Applicants submit that the use of those pyrilamine tannate and phenylephrine tannate forms, as in the Chopdekar patents, results in compositions that exhibit greater variability of active ingredients in each batch or dosage unit of the final drug composition product as compared to the presently claimed composition prepared by the method recited in those claims. In fact, the Chopdekar patents say as much themselves in that the Chopdekar patents describe that the water remaining following preparation of the tannate salts must be removed by a freeze-drying step, and any further water remaining is an impurity that requires an adjustment of each dosage (*see* col. 1, line 67 through col. 2, line 2; col. 2, lines 11-13; and col. 3, lines 11-30 of the Chopdekar '846 patent, and col. 1, line 67 through col. 2, line 3; col. 2, lines 14-16; and col. 3, lines 11-28 of the Chopdekar '415 patent). The presently claimed composition is completely different from that formed by the process of the Chopdekar patents. Since it is converted in situ into the tannate form and then directly into suspension, there is no water as an impurity, and the separate dispersion promotes homogeneity of the active pharmaceutical ingredients, thereby requiring no adjustment of dosages. This is wholly unlike a composition formed by the process of the Chopdekar patents, such as the composition of Venkataraman.

The general cause of increased content variability that is inherently produced using the prior art methods of the Chopdekar patents is not difficult to explain. Each step or operation performed in a manufacturing environment introduces some

level of variability into the finished product. When the operation in question, such as a method of the Chopdekar patents, involves isolating a tannate salt, such as by beginning with the free-base form and then converting to the tannate salt, and thereafter processing those tannate salts into a composition, the variability is focused on the amount of active ingredient contained in the finished pharmaceutical product. By eliminating the additional isolation step required by the prior art that is a potential source of increased content variability, the compositions presently claimed by the recited process are able to provide a consistently better finished product.

The decreased content variability that results in the claimed compositions due to the recited method has many real world advantages. A better finished in the pharmaceutical industry means a safer drug. The principal property affected by converting a drug to the tannate salt form is solubility, which normally decreases after conversion to a tannate from a hydrochloride salt or bromide salt. The decreased solubility attained in this matter gives the drug prolonged action characteristics. Changes in the content of the tannate salt in a final drug product can potentially alter the overall amount of drug taken, as well as the rate at which the drug enters the body. Understandably, then, increased variability in drug content leads to increased risk to the patient taking the drug product. The need for increased safety and content uniformity is multiplied by the fact that many of the tannate drug products are designed for use by children.

Applicants submit that since this homogeneity is generated by the particular process of the claimed invention, the differing steps of the present process over that of the prior art provide for differences in the compositions that are formed by the respective processes: namely, that each dosage unit formed includes amounts of active pharmaceutical ingredients that are homogeneous when compared to all other dosage units formed. Applicants further assert that since the Chopdekar patents do not disclose the process steps necessary to generate such homogeneity of active pharmaceutical ingredients, compositions produced by the method of the Chopdekar patents, such as those of Venkataraman, do not exhibit such homogeneity. Thus, in the present invention, the method changes the product over that found in the cited art. As a result, Applicants submit that, based on the method, the claimed product is patentable over the cited art.

Applicants note that neither Venkataraman nor the Chopdekar patents disclose the process by which the homogeneity of active pharmaceutical ingredient in the present composition is achieved. In fact, as previously noted, Venkataraman and the Chopdekar patents only describe the "old" routes of preparation, which Applicants describe in the application as forming compositions which vary in the amount of active pharmaceutical ingredient from dosage unit to dosage unit. Thus, Applicants submit that the composition disclosed in Venkataraman, produced by conventional methods, such as the methods of the Chopdekar patents, will not exhibit such homogeneity, and

rather disclose compositions that exhibit variable levels of active pharmaceutical ingredient from dosage unit to dosage unit of the composition. As a result, Applicants submit that it cannot be the case that the composition disclosed in Venkataraman is the same as the composition claimed in the present application.

In view of the above, Applicants assert that Venkataraman does not teach all the limitations of independent claims 1 and 53 as presently amended, and further assert that the process of the independent claims renders a different product than the process described in Venkataraman or the Chopdekar patents. As such, Applicants respectfully request a withdrawal of the rejection of claims 1, 3-8, 10-18, 21, and 53 under 35 U.S.C. § 102.

Claim Rejections 35 U.S.C. § 103

The Examiner has rejected claims 1-21 and 53 under 35 U.S.C. § 103(a) as being unpatentable over Venkataraman. The Examiner states that the difference between Venkataraman and the presently claimed subject matter lies in that the reference fails to teach the presently claimed weight percentage or milligram dosage amounts of the active pharmaceutical ingredients of the composition or the pH of the composition between 3.5 and 6.5. Applicants respectfully disagree.

Applicants first note that any presently claimed weight percentage or milligram dosage amounts of the active pharmaceutical ingredients of the composition, or the pH of the composition being between 3.5 and 6.5, is not found in any of the

independent claims presently pending, or as originally filed. Rather, those limitations are only found in dependent claims. Regardless, as noted above, claims 1 and 53 as presently amended produce a composition by a completely different process than that described in Venkataraman (or the Chopdekar patents), which results in a composition that is wholly different than that described in Venkataraman. Nowhere do Venkataraman or the Chopdekar patents disclose or suggest a process that would result in the different product of the present application. In fact, as described above, Venkataraman only recites conventional methods of preparing the composition, and the Chopdekar patents, incorporated by reference into Venkataraman, only teach those old conventional methods, which are the very methods listed as a drawback in the Background section of the present application, and which the present application is specifically directed away from. Thus, Applicants respectfully request withdrawal of the rejection of claims 1-21 and 53 under 35 U.S.C. § 103(a).

Claim Rejections Double Patenting

Claims 1-21 and 53 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-21, 31-48, and 53 of copending Application 10/047,578. In view of the claims as presently amended, Applicants respectfully disagree.

Applicants first note that each independent claim 1, 31, and 53 has been presently amended to recite active pharmaceutical ingredients "consisting essentially of"

phenylephrine, pyrilamine, and dextromethorphan. Thus, Applicants respectfully disagree with the Examiner's statement that the interpretation of the present claims allows for the inclusion of any other unspecified components by reciting "comprising." Thus, Applicants submit that the inclusion of dextromethorphan in the claims of the present application renders the present claim as nonobvious over copending Application 10/047,578. Applicants therefore respectfully request a withdrawal of the rejection of claims 1-21 and 53 under the judicially created doctrine of obviousness-type double patenting.

Conclusion

For the foregoing reasons, it is submitted that all claims are patentable, and a Notice of Allowance is respectfully requested.

Please consider this paper a Petition for an Extension of Time of three months, and charge the appropriate fee of $510.00 under 37 CFR 1.17(a)(3) to Deposit Account 23-3000. Any deficiencies or credits necessary to complete this communication should be applied to Deposit Account No. 23-3000.

The Examiner is invited to contact the undersigned attorney with any questions or remaining issues.

Respectfully submitted,
WOOD, HERRON & EVANS, L.L.P.

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